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(17376 BOT)

PATENT

REMARKS

I. Claim status

Upon entry of the above amendments, claims 1-7 and 9-15 will be pending in this application. Claims 1-7 have been amended. Support for the amendments can be found throughout the specification (e.g., Tables 1 and 2 on pages 19-21; and page 21, lines 20-35; page 22, lines 5 to 12), and in the original claims. Claims 9-15 have been added. Support for the added claims can be found throughout the specification (e.g., Tables 1 and 2 on pages 19-21 of the specification) and in the original claims. No new matter has been added.

II. Sequence Listing

The specification has been amended to provide sequence identifiers to all amino acid sequences of at least 4 amino acids. The identifiers are consistent with the computer readable sequence listing previously submitted.

III. The claims are fully described by the specification

Claims 1-7 were rejected under 35 U.S.C. § 112, paragraph 1, as allegedly lacking written description. Specifically, the Examiner stated that "a 'modified neurotoxin' alone is insufficient to describe a genus." Contrary to the Examiner's allegation, the genus of modified neurotoxins of the claims is not simply identified as a "modified neurotoxin", or as amended, "modified botulinum toxin." The recited modified botulinum toxins of each pending claim have common distinguishing attributes. For example, independent claim 1 recites a modified botulinum toxin comprising at least one phosphorylation site as a secondary modification site. Further, the various phosphorylation sites that may be employed in accordance with claim 1 are identified, for example, on Table 1 and 2 on pages 19-21 of the specification. Independent claim 2 recites a modified botulinum toxin comprising one or more secondary modification sites. Accordingly, the distinguishing attributes shared by member botulinum toxin of claim 2 are that they comprise secondary

modification sites. Further, numerous examples of secondary modification sites are identified throughout the specification, for example, Tables 1 and 2.

Since the claims are fully described, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, paragraph 1.

IV. The claims are novel

WO 96/39166 (Johnson et al.):

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Johnson et al. Applicants respectfully traverse the rejection because Johnson et al. fails to teach or suggest all the features of the present invention. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995).

The present claims are directed to botulinum toxins that have secondary modification sites "which may be *targeted* by an enzyme, for example an intracellular enzyme, to affect a modification to the site, for example phosphorylation, glycosylation, etc." Page 14, lines 19-25 of the specification. For example, amended claim 2 recites a modified botulinum toxin comprising a one or more "secondary modification sites" in addition to the ones that are already naturally present on a neurotoxin. The secondary modification sites include posttranslational N-glycosylation, casein kinase II (CK-2) phosphorylation, N-terminal myristylation, protein kinase C (PKC) phosphorylation and tyrosine phosphorylation sites (e.g., claims 3, 6 and 7). The modified botulinum toxin may also be the devoid of the secondary modification sites, e.g., said posttranslational modification sites (e.g., claims 4 and 5).

Johnson et al. does not disclose a modified neurotoxin comprising a secondary modification site that may be the *target of an enzyme* for secondary modification, much less any particular secondary modification site such as phosphorylation site, glycosylation site, etc. Instead, Johnson et al. merely reports a botulinum toxin analogue having a more stable acid residue in a pairing at a degradable site. Specifically, Johnson et al. reports that such botulinum toxin analogues have a threonine residue in place of a

tyrosine residue, or an asparagine residue in place of an arginine residue, at the degradable site. Further, Johnson et al. does not disclose or teach that these substitutions will cause an enzyme to target these substituted sites to affect a secondary modification (e.g., phosphorylate) to the botulinum toxin.

Because Johnson et al. fails to teach or suggest every feature of the invention, the claims are not anticipated. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(b).

U.S. Patent Number 5,837,265 (Montal et al.)

Claims 1-7 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Montal et al. Applicants respectfully traverse the rejection because Montal et al. fails to teach or suggest all the features of the present invention. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995).

As discussed above, the present claims are directed to botulinum toxins that have secondary modification sites. Further, the presently claimed modified botulinum toxins have secondary modification sites that are in *addition* to the ones that are naturally occurring on the unmodified botulinum toxin.

Montal et al., on the other hand, reports a phosphorylated toxin. The phosphorylation itself is *not* a secondary modification site. In other words, a phosphorylation itself is not an amino acid sequence region (secondary modification site) "which may be *targeted* by an enzyme, for example an intracellular enzyme, to affect a modification to the site, for example phosphorylation, glycosylation, etc." Page 14, lines 19-25 of the specification. Further, Montal et al. does not disclose, teach or even suggest a modified botulinum toxin having a secondary modification site (enzymatic target) in *addition* to the naturally occurring ones. At most, Montal et al. discloses how to phosphoryate an unmodified botulinum toxin. See Example 1 entitled "Enzymatic Phosphorylation of BoTx and TeTx Tyrosines by pp60" at Col 9, lines 60 to Col 11, line 41. Since Montal et al. does not disclose all the features of the present claims (e.g.,

secondary modification sites in addition to the ones on unmodified botulinum toxins), Montal et al. cannot anticipate the claims.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(b).

V. Conclusion

In view of the foregoing, Applicant submits that the claims as amended and new claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,

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